PATENT COOPERATION TREATY

From the INTERNATIONAL SEARCHING AUTHORITY

PCT

To:
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DOCKETED

Feb. 26, 2009 - 2 week reminder
Mar. 12, 2009 - Pay Additional Fees - Deadline

REGISTERED MAIL

INVITATION TO PAY ADDITIONAL FEES AND, WHERE APPLICABLE, PROTEST FEE

ticle 17(3)(a) and Rule 40.1 and 40.2(e))

	Date of mailing *(day/month/year)* 12/02/2009
Applicant's or agent's file reference CDJ-346PC	**PAYMENT DUE** within **ONE MONTH** from the above date of mailing
International application No. PCT/US2008/082745	International filing date *(day/month/year)* 07/11/2008
Applicant CELLDEX THERAPEUTICS INC.	

1. This International Searching Authority

(i) considers that there are 9 *(number of)* inventions claimed in the international application covered by the claims indicated on an extra sheet:

(ii) therefore considers that **the international application does not comply with the requirements of unity of invention** (Rules 13.1, 13.2 and 13.3) for the reasons indicated on an extra sheet:

(iii) [X] has carried out a partial international search (see Annex) [ ] will establish the international search report on those parts of the international application which relate to the invention first mentioned in claims Nos.:

see extra sheet

(iv) will establish the international search report on the other parts of the international application only if, and to the extent to which, additional fees are paid.

2. Consequently, the applicant is hereby **invited to pay,** within the time limit indicated above, the amount indicated below:

EUR 1,700,00	x	8	=	EUR 13,600
Fee per additional invention		number of additional inventions		currency/total amount of additional fees

3. The applicant is informed that, according to Rule 40.2(c), **the payment of any additional fee may be made under protest,** i.e., a reasoned statement to the effect that the international application complies with the requirement of unity of invention or that the amount of the required additional fee is excessive, where applicable, subject to the payment of a protest fee.

Where the applicant pays additional fees under protest, the applicant is hereby invited, within the time limit indicated above, to pay a protest fee (Rule 40.2(e)) in the amount of EUR 750,00 *(currency/amount)*

Where the applicant has not, within the time limit indicated above, paid the required protest fee, the protest will be considered not to have been made and the International Searching Authority will so declare.

4. [ ] Claim(s) Nos. _____ have been found to be unsearchable under Article 17(2)(b) because of defects under Article 17(2)(a) and therefore have not been included with any invention.

Name and mailing address of the International Searching Authority European Patent Office, P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Authorized officer Julia Severin

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Form PCT/ISA/206 (April 2005)

Annex to Form PCT/ISA/206
COMMUNICATION RELATING TO THE RESULTS OF THE PARTIAL INTERNATIONAL SEARCH

International Application No
PCT/US2008/082745

1. The present communication is an Annex to the invitation to pay additional fees (Form PCT/ISA/206). It shows the results of the international search established on the parts of the international application which relate to the invention first mentioned in claims Nos.:
see 'Invitation to pay additional fees'
2. This communication is not the international search report which will be established according to Article 18 and Rule 43.

3. If the applicant does not pay any additional search fees, the information appearing in this communication will be considered as the result of the international search and will be included as such in the international search report.

4. If the applicant pays additional fees, the international search report will contain both the information appearing in this communication and the results of the international search on other parts of the international application for which such fees will have been paid.

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 2004/035619 A (CENTENARY INST CANCER MEDICINE [AU]; BRITTON WARWICK [AU]; DEMANGEL CA) 29 April 2004 (2004-04-29) page 40 - page 48 figure 3A	1-4,6-84
X	BADIEE ET AL: "Enhanced delivery of immunoliposomes to human dendritic cells by targeting the multilectin receptor DEC-205" VACCINE, BUTTERWORTH SCIENTIFIC. GUILDFORD, GB, vol. 25, no. 25, 30 May 2007 (2007-05-30), pages 4757-4766, XP022098619 ISSN: 0264-410X figures 3-6 page 4758, right-hand column, paragraph 4 - page 4759, left-hand column, paragraph 1 page 4761 page 4765, left-hand column, paragraph 3 - right-hand column, paragraph 2	1-4,6-84

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[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	GUO M ET AL: "A monoclonal antibody to the DEC-205 endocytosis receptor on human dendritic cells" HUMAN IMMUNOLOGY, NEW YORK, NY, US, vol. 61, no. 8, 1 August 2000 (2000-08-01), pages 729-738, XP002319045 ISSN: 0198-8859 page 730, right-hand column, paragraph 2 page 732, right-hand column, paragraph 2 figures 2,4-6	1-4,6-84
X	US 2005/186612 A1 (HART DEREK N [NZ]) 25 August 2005 (2005-08-25) paragraph [0114] figure 9	1-4,6-84
X	WO 2004/074432 A (MEDAREX INC [US]; KELER TIBOR [US]; ENDRES MICHAEL [US]; HE LIZHEN [US) 2 September 2004 (2004-09-02) page 34, line 16 - page 39, line 17 figures 9,14	1-4,6-84
A	WO 2005/018610 A (LIPOTEK PTY LTD [AU]; ALTIN JOSEPH [AU]; PARISH CHRISTOPHER RICHARD [A) 3 March 2005 (2005-03-03) page 20, line 15 - page 23, line 20	1-4,6-84
A	US 2004/258688 A1 (HAWIGER DANIEL [US] ET AL) 23 December 2004 (2004-12-23) paragraphs [0356], [0378] - [0389] figures 10-12	1-4,6-84

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INVITATION TO PAY ADDITIONAL FEES

International application No.
PCT/US2008/082745

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 15, 24, and 28 (all fully), 1-4,6-14,16-23,25-27 and 29-84 (all partially)

An isolated monoclonal antibody which binds to human DEC-205 and comprises heavy and light chain variable region CDR1, CDR2 and CDR3 sequences selected from the group consisting of a heavy chain variable region CDR1 comprising SEQ ID NO.29, a heavy chain variable region CDR2 comprising SEQ ID NO.30, a heavy chain variable region CDR3 comprising SEQ ID NO.31, a light chain variable region CDR1 comprising SEQ ID NO.35, a light chain variable region CDR2 comprising SEQ ID NO.36, and a light chain variable region CDR3 comprising SEQ ID NO.37. An isolated monoclonal antibody which binds to human DEC-205 and comprises a heavy and light chain variable region comprising SEQ ID NOs: 28 and 34 respectively.

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2. claims: 1-4,6-14,16-23,25-27 and 29-84 (all partially)

Idem as invention 1, wherein the heavy and light chain CDR1-3 comprise SEQ ID NOs:5-7 and 11-13 respectively, and the heavy and light chain variable regions comprise SEQ ID NOs: 4 and 10 respectively.

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3. claims: 1-4,6-14,16-23,25-27 and 29-84 (all partially)

Idem as invention 1, wherein the heavy and light chain CDR1-3 comprise SEQ ID NOs:17-19 and 23-25 respectively, and the heavy and light chain variable regions comprise SEQ ID NOs: 16 and 22 respectively.

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4. claims: 1-4,6-14,16-23,25-27 and 29-84 (all partially)

Idem as invention 1, wherein the heavy and light chain CDR1-3 comprise SEQ ID NOs:41-43 and 47-49 respectively, and the heavy and light chain variable regions comprise SEQ ID NOs: 40 and 46 respectively.

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5. claims: 1-4,6-14,16-23,25-27 and 29-84 (all partially)

Idem as invention 1, wherein the heavy and light chain CDR1-3 comprise SEQ ID NOs:53-55 and 59-61 respectively, and the heavy and light chain variable regions comprise SEQ ID NOs: 52 and 58 respectively.

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6. claims: 1-4,6-14,16-23,25-27 and 29-84 (all partially)

Idem as invention 1, wherein the heavy and light chain CDR1-3 comprise SEQ ID NOs:77-79 and 83-85 respectively, and the heavy and light chain variable regions comprise SEQ ID NOs: 76 and 82 respectively.

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7. claims: 1-4,6-9,12,13,16,21,25,29,31-33,35-84 (all partially)

An isolated monoclonal antibody which binds to human DEC-205 and comprises a heavy chain variable region comprising SEQ ID NO: 88.

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8. claims: 1-3,5-9,12,13,16,21,25,29,31-33,35-84 (all partially)

An isolated monoclonal antibody which binds to human DEC-205 and comprises a heavy chain variable region comprising SEQ ID NO: 64.

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9. claims: 1-3,5-9,12,13,16,21,25,29,31-33,35-84 (all partially)

An isolated monoclonal antibody which binds to human DEC-205 and comprises a heavy chain variable region comprising SEQ ID NO: 70.

The underlying application relates to antibodies to human DEC205. Such antibodies are known in the art. For instance, WO2004035619 discloses the sequence of a rat anti DEC-205 monoclonal antibody termed NLDC-145 (ATCC Accession No. HB-2990), wherein the variable heavy chain CDR3 sequence RYFDL falls in the consensus (core) variable heavy chain CDR3 of the antibodies of the underlying application (compare Figure 3A with Figure 6 of the underlying application). Guo et al. (XP002319045) discloses the production of a murine monoclonal antibody termed MG38 against the cysteine-rich and fibronectin II domain of human DEC-205, wherein the antibody does not recognize murine DEC-205 (page 730, righthand column, par 2, page 732, righthand column, par 2 and Figures 2,4,5 and 6). US20050186612 discloses monoclonal antibodies raised in mice to two peptides derived from the human DEC205 sequence (residues 1267-1277 and 1227-123), see par 114 and Figure 9. WO2004074432 discloses a fully human antibody termed B11 specific for the mannose receptor on dendritic cells, wherein the light chain variable region is identical to the antibody heavy chain 2F4 of the current application (compare the variable chain, CDR1-3 and the germline L15 in Figures 9 and 14 with Figure 5 of the current application). The antibody was fused to the human chorionic gonadotropin antigen and the conjugate used to stimulate T cell responses (page 34, line 16-page39, line 17).

In the light of the prior art , the problem to be solved may therefore be defined as the provision of further antibodies to human DEC205. The following solutions are provided in the claims:

Inventions 1-9, as defined supra.

Since the monoclonal antibodies to human DEC205 are known in the art, the application does not contain a single general inventive concept as required to be present by Article 3(4)(iii) and Rule 13.1 PCT. When considering the whole set of claims in the light of the description, no further technical features could be identified which could serve as same or corresponding technical features in the sense of Rule 13.2 PCT to restore unity of invention. The fact that antibodies disclosed in the examples contain human germline sequences, cannot provide for a single general inventive concept, since the provision of human antibodies to a known antigen which has been already demonstrated to play a causative role in human pathologies is an activity which does not require inventive skills. When considering the structural features of the antibodies, the ISA is of the opinion that there are no structural features in common between Inventions 1-9 involving different sequences and different combinations of sequences which may represent the technical feature in the sense of Rule 13.2 PCT. Furthermore, it appears that there are no functional features which are common for all or some of the claimed solutions which may serve as the special technical feature in the sense of Rule 13.2 PCT. Consequently, the requisite unity of invention (Rule 13.1 PCT) therefore no longer exists inasmuch as a technical relationship involving one or more of the same or corresponding special technical features in the sense of Rule 13.2 PCT does not exist between the subject-matter of the groups of claims.

Patent Family Annex

Information on patent family members

International Application No
PCT/US2008/082745

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 2004035619 A	29-04-2004	AU 2003271430 A1	04-05-2004
US 2005186612 A1	25-08-2005	NONE	
WO 2004074432 A	02-09-2004	AU 2004213749 A1	02-09-2004
		CA 2514979 A1	02-09-2004
		CN 1767852 A	03-05-2006
		EP 1594533 A2	16-11-2005
		JP 2006516637 T	06-07-2006
		NZ 541903 A	29-08-2008
WO 2005018610 A	03-03-2005	CN 1893925 A	10-01-2007
		EP 1660040 A1	31-05-2006
		JP 2007502780 T	15-02-2007
		US 2007026057 A1	01-02-2007
US 2004258688 A1	23-12-2004	NONE	